

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to:

Attorney Docket No.: 019801-000230US PATENT

Assistant Commissioner for Patents
Washington, D.C. 20231

On August 21, 2001
TOWNSEND and TOWNSEND and CREW LLP
By: Jay M. Marshall

RECEIVED
OCT 08 2002
TECH CENTER 1600/2900

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:

Rothbard, et al.

Application No.: 09/792,480

Filed: February 23, 2001

For: COMPOSITIONS AND METHODS
FOR ENHANCING DRUG DELIVERY
ACROSS AND INTO EPITHELIAL
TISSUES

Examiner: Not assigned

Art Unit: 1615

INFORMATION DISCLOSURE
STATEMENT UNDER 37 CFR §1.97 and
§1.98

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

The references cited on attached form PTO-1449 are being called to the attention of the Examiner. Copies of the references are enclosed. Also enclosed is a copy of the Search/Examination report corresponding to a related PCT application. It is respectfully requested that the cited references be expressly considered during the prosecution of this application, and the references be made of record therein and appear among the "references cited" on any patent to issue therefrom.

Application No.: 09/792,480

Page 2

As provided for by 37 CFR 1.97(g) and (h), no inference should be made that the information and references cited are prior art merely because they are in this statement and no representation is being made that a search has been conducted or that this statement encompasses all the possible relevant information.

Applicant believes that no fee is required for submission of this statement, since it is being submitted prior to the first Office Action. However, if a fee is required, the Commissioner is authorized to deduct such fee from the undersigned's Deposit Account No. 20-1430. Please deduct any additional fees from, or credit any overpayment to, the above-noted Deposit Account.

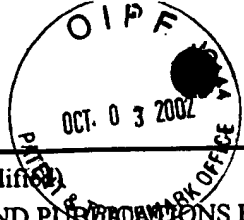
Respectfully submitted,



Matthew E. Hinsch
Reg. No. 47,651

TOWNSEND and TOWNSEND and CREW LLP
Two Embarcadero Center, 8th Floor
San Francisco, California 94111-3834
Tel: 415-576-0200
Fax: 415-576-0300
MEH:jmm

SF 1261047 v1



FORM PTO-1449 (Modified) LIST OF PATENTS AND PUBLICATIONS FOR APPLICANT'S INFORMATION DISCLOSURE STATEMENT (Use several sheets if necessary)	Attorney Docket No.: 019801-000230US Applicant: Rothbard, et al. Filing Date: February 23, 2001	Application No.: 09/792,480 Group: 1615
---	--	--

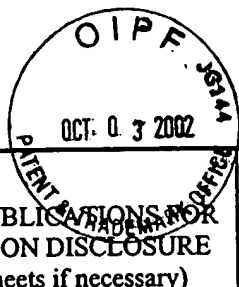
Reference Designation	U.S. PATENT DOCUMENTS	Page 1
------------------------------	------------------------------	---------------

Examiner Initial	Document No.	Date	Name	Class	Sub-class	Filing Date (If Appropriate)
1	4,880,911	11/14/89	Brewer, et al.			
2	4,847,240	7/11/89	Ryser, et al.			
3	4,701,521	10/20/87	Ryser, et. al.			
4	4,631,190	12/23/86	Shen, et. al.			
5	4,532,207	7/30/85	Brewer, et. al.			
6	5,783,178	7/21/98	Kabanov, et al.			
7	5,795,909	8/18/98	Shashoua			
8	5,831,001	11/03/98	Twist, et al.			
9	5,789,531	8/04/98	Sumner-Smith, et al.			
10	5,716,614	2/10/98	Katz, et al.			
11	5,674,849	10/07/97	Twist, et al.			
12	5,646,120	07/08/97	Sumner-Smith, et al.			
13	5,633,230	05/27/97	Twist, et al.			
14	5,354,844	10/11/94	Beug, et al.			
15	5,162,505	11/10/92	Dean, et al.			
16	5,804,604	09/08/98	Frankel, et al.			
17	5,362,831	11/08/94	Mongelli, et al.			
18	5,028,707	07/02/91	Nichols, et. al.			
19	4,046,722	09/06/77	Rowland			
20	5,977,163	11/02/99	Li, et al.			
21	6,077,835	06/20/00	Hanson, et al.			

FOREIGN PATENT DOCUMENTS

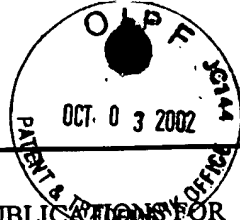
	Document No.	Date	Country	Class	Sub-class	Translation (Yes/No)
22	2,094,658	10/24/93	Canada			
23	EP 0009498	06/27/84	Europe			
24	WO 91/09958	07/11/91	PCT			
25	WO 98/52614	11/26/98	PCT			
26	EP 0 599 303	06/01/94	Europe			
27	WO 97/40854	11/06/97	PCT			
28	WO 97/33552	09/18/97	PCT			
29	WO 96/21036	07/11/96	PCT			
30	WO 95/11038	04/27/95	PCT			
31	WO 94/14464	07/07/94	PCT			
32	WO 94/04686	03/03/94	PCT			
33	WO 93/21941	11/11/93	PCT			

FORM PTO-1449 (Modified) LIST OF PATENTS AND PUBLICATIONS FOR APPLICANT'S INFORMATION DISCLOSURE STATEMENT (Use several sheets if necessary)				Attorney Docket No.: 019801-000230US		Application No.: 09/792,480	
				Applicant: Rothbard, et al.			
				Filing Date: February 23, 2001		Group: 1615	
34	WO 93/04701	03/18/93	PCT				
35	WO 92/07871	05/14/92	PCT				
36	WO 91/09958	07/11/91	PCT				
37	WO 79/00515	08/09/79	PCT				
38	WO 01/13957	03/01/01	PCT				
39	GB 744 988	02/15/56	Germany				
40	JP 10 095738	04/14/98	Japan				
OTHER ART (Including Author, Title, Date, Pertinent Pages, Etc.)							
41	Arbus, et al. "Taxol: Clinical Results and Current Issues in Development"; Chapter 14 in <i>TAXOL®: Science and Applications</i> , M. Suffness ed., CRC Press (New York), p. 379-415 (1995)						
42	Balicki, et al. "Histone H2A Significantly Enhances In Vitro DNA Transfection"; <i>Molecular Medicine</i> Vol. 3, No. 11 p. 782-787 (1997)						
43	Boussif, et al. "A versatile vector for gene and oligonucleotide transfer into cells in culture and <i>in vivo</i> : Polyethylenimine"; <i>Proc. Natl. Acad. Sci. USA</i> Vol. 92, p. 7297-7301 (August 1995)						
44	Burton, et al. "Basic polyelectrolytes and protein transport across the new-born pig intestine"; <i>Physiological Society</i> p. 27P-28P (Sep. 1970)						
45	Brigidou, et al. "The <i>Retro-Inverso</i> Form of a Homeobox-Derived Short Peptide is Rapidly Internalised by Cultured Neurons: A New Basis For An Efficient Intracellular Delivery System"; <i>Biochemical and Biophysical Research Communications</i> Vol. 214, No. 2 p. 685-693 (Sep. 1995)						
46	Buschle, et al. "Transloading of tumor antigen-derived peptides into antigen-presenting cells"; <i>PNAS</i> Vol. 94, p. 3256-3261 (April 1997)						
47	Chen, et al. "Galactosylated Histone-Mediated Gene Transfer and Expression"; <i>Human Gene Therapy</i> Vol. 5, p. 429-435 (1994)						
48	Cooke, et al. "NITRIC OXIDE SYNTHASE: Role in the Genesis of Vascular Disease"; <i>Annu. Rev. Med.</i> Vol. 48, p. 489-509 (1997)						
49	Dattilo, et al. "Inducible Nitric Oxide Synthase Expression in Human Vein Grafts"; <i>Am J Surg.</i> Vol. 174, p. 177-180 (1997)						
50	de Bont, et al. "Synthesis and Biological Activity of β -Glucuronyl Carbamate-Based Prodrugs of Paclitaxel as Potential Candidates for ADEPT"; <i>Bioorganic & Medicinal Chemistry</i> Vol. 5, No. 2 p. 405-414 (1997)						
51	Derossi, et al. "The Third Helix of the Antennapedia Homeodomain Translocates through Biological Membranes"; <i>The Journal of Biological Chemistry</i> Vol. 269, No. 14 p. 10444-10450 (1994)						
52	Elferink, "Changes of Plasma Membrane Permeability in Neutrophils Treated With Polycations"; <i>Inflammation</i> Vol. 15, No. 2 p. 103-115 (Apr. 1991)						
53	Emi, et al. "Gene Transfer Mediated by Polyarginine Requires a Formation of Big Carrier-Complex of DNA Aggregate"; <i>Biochemical and Biophysical Research Communications</i> Vol. 231, p. 421-424 (1997)						
54	Fawell, et al. "Tat-mediated delivery of heterologous proteins into cells"; <i>Proc. Natl. Acad. Sci. USA</i> Vol. 91, p. 664-668 (Jan. 1994)						
55	Fletcher, et al. "Partially Modified Retro-Inverso Peptides: Development, Synthesis, and Conformational Behavior"; <i>Chem. Rev.</i> Vol. 96 p. 763-795 (1998)						
56	Garg, et al. "Nitric Oxide-generating Vasodilators and 8-Bromo-Cyclic Guanosine Monophosphate Inhibit Mitogenesis and Proliferation of Cultured Rat Vascular Smooth Muscle Cells"; <i>J. Clin. Invest.</i> Vol. 83, p. 1774-1777 (May 1989)						
57	Georg, et al. "The Medicinal Chemistry of Taxol"; Chapter 13 in <i>TAXOL®: Science and Applications</i> , M. Suffness ed., CRC Press (New York), p. 317-375 (1995)						



FORM PTO-1449 (Modified)		Attorney Docket No.: 019801-000230US	Application No.: 09/792,480
LIST OF PATENTS AND PUBLICATIONS FOR APPLICANT'S INFORMATION DISCLOSURE STATEMENT (Use several sheets if necessary)		Applicant: Rothbard, et al.	
		Filing Date: February 23, 2001	Group: 1615

58	Golik, et al. "Synthesis and Antitumor Evaluation of Paclitaxel Phosphonooxymethyl Ethers: A Novel Class of Water Soluble Paclitaxel Pro-Drugs" <i>Bioorganic & Medicinal Chemistry Letters</i> Vol. 6, No. 15 p. 1837-1842 (1996)
59	Greenwald, et al. "Drug Delivery Systems: Water Soluble Taxol 2'-Poly(ethylene glycol) Ester Prodrugs-Design and <i>in Vivo</i> Effectiveness"; <i>J. Med. Chem.</i> 39(2):424-431 (Jan. 1996)
60	Kessler "Peptoids-A New Approach to the Development of Pharmaceuticals"; <i>Angew Chem. Int. Ed. Engl.</i> Vol. 32, No. 4 p. 543-544 (1993)
61	Kingston "Natural Toxoids: Structure and Chemistry"; Chapter 12 in <i>TAXOL®: Science & Applications</i> , M. Suffness ed, CRC Press (New York), p. 287-315 (1995)
62	Lam, et al. "The "One-Bead-One-Compound" Combinatorial Library Method"; <i>Chem. Rev.</i> Vol. 97, p. 411-448 (1997)
63	Lloyd-Jones, M.D., et al. "The Vascular Biology of Nitric Oxide and Its Role in Atherogenesis"; <i>Annu. Rev. Med.</i> Vol. 47, p. 365-375 (1996)
64	Mauersberger, et al. "Untersuchungen zur Zytotoxizität von Poly-L-Arginin, Poly-L-Lysin und DEAE-Dextran bei L-Zellen und Mäuseembryofibroblasten"; <i>Exp. Path.</i> Vol. 18 p. 268-274 (1977)
65	Murphy, et al. "A combinatorial approach to the discovery of efficient cationic peptoid reagents for gene delivery"; <i>Proc. Natl. Acad. Sci. USA</i> Vol. 95, p. 1517-1522 (Feb. 1998)
66	Natsume, et al. "Screening of Absorption Enhancers for Nasal Peptide and Protein Delivery"; <i>Proceed. Intern. Symp. Control. Rel. Bioact. Mater.</i> Vol. 23, P. 481-482 (July 1996)
67	Nicolaou, et al. "Design, synthesis and biological activity of protaxols"; <i>Nature</i> Vol. 364, p. 464-466 (July 1993)
68	Rodrigues, et al. "Synthesis and β -lactamase-mediated activation of a cephalosporin-taxol prodrug" <i>Chemistry and Biology</i> Vol. 2, p. 223-227 (Apr. 1995)
69	Rose, "Preclinical Antitumor Activity of Taxanes"; Chapter 8 in <i>TAXOL®: Science & Applications</i> , M. Suffness ed., CRC Press (New York), p. 209-235 (1995)
70	Simon, et al. "Peptoids: A modular approach to drug discovery"; <i>Proc. Natl. Acad. Sci. USA</i> Vol. 89 p. 9367-9371 (Oct. 1992)
71	Straubinger "Biopharmaceutics of Paclitaxel (Taxol): Formulation, Activity, and Pharmacokinetics"; Chapter 9 in <i>TAXOL® Science and Applications</i> , M. Suffness ed., CRC Press (New York), p. 237-258 (1995)
72	Sumner-Smith, et al. "123: 79357m Antiherpetic activities of N- α -acetyl-nona-D- ϵ -arginine amide acetate"; <i>6001 Chemical Abstracts</i> Vol. 123, No. 7 p. 606 (1995)
73	Thompson, et al. "Synthesis and Applications of Small Molecule Libraries"; <i>Chem. Rev.</i> 96:555-600 (1996)
74	Tsao, et al. "Nitric Oxide Regulates Monocyte Chemotactic Protein-1"; <i>Circulation</i> 96: 934-940 (1997)
75	Uchida, et al. "Polycations Decrease the Transepithelial Resistance of Cultured Tracheal Epithelial Cells"; <i>Chest</i> Vol. 101, No. 3, p. 33S (March 1992)
76	Ueda, et al. "Synthesis and Antitumor Evaluation of 2'-Oxycarbonylpaclitaxels (Paclitaxel-2'-Carbonates)"; <i>Bioorganic & Medicinal Chemistry Letters</i> Vol. 4 No. 15 p. 1861-1864 (Aug. 1994)
77	Ueda, et al. "Novel Water Soluble Phosphate Prodrugs of Taxol® Possessing <i>In Vivo</i> Antitumor Activity"; <i>Bioorganic & Medicinal Chemistry Letters</i> Vol. 3, No. 8:1761-1766 (May 1993)
78	Vyas, et al. "Synthesis and Antitumor Evaluation of Water Soluble Taxol Phosphates"; <i>Bioorganic & Medicinal Chemistry Letters</i> Vol. 3, No. 6 p. 1357-1360 (1993)
79	Vyas, et al. "Phosphatase-Activated Prodrugs of Paclitaxel"; Chapter 9 in <i>Taxane Anticancer Agents</i> American Chemical Society p. 124 (1995)
80	Wolf, et al. "Dietary L-Arginine Supplementation Normalizes Platelet Aggregation in Hypercholesterolemic Humans"; <i>JACC</i> Vol. 29, No. 3 p. 479-485 (March 1997)
81	Zuckermann, et al. "Efficient Method for the Preparation of Peptoids [Oligo(N-substituted glycines)] by Submonomer Solid-Phase Synthesis"; <i>Chemtracts-Macromolecular Chemistry</i> Vol. 4 p. 80-83 (1993)
82	Aoyagi, et al. "Polymerization of Benzalkonium Chloride-Type Monomer and Application to Percutaneous Drug Absorption Enhancer"; <i>Journal of Controlled Release</i> , Vol 13, No. 1 pp. 63-71 (July 1990)



PUBLICATIONS FOR ION DISCLOSURE (sheets if necessary)	Attorney Docket No.: 019801-000230US	Application No.: 09/792,480
	Applicant: Rothbard, et al.	
	Filing Date: February 23, 2001	Group: 1615
l., "Cutaneous vaccination: the skin as an immunologically active tissue and the challenge of antigen <i>Journal of Controlled Release</i> Vol. 66 pp. 199-214 (2000)		
"Liposomes enhance delivery and expression of an RGD-oligolysine gene transfer vector in human ls"; <i>Gene Therapy</i> Vol. 5 pp. 1488-1498 (1998)		
. "Role of Cationic Proteins in the Airway Hyperresponsiveness Due to Airway Inflammation"; <i>Am.</i> <i>t. Care Med.</i> Vol. 150 pp. 563-571 (1994)		
. "Ca ²⁺ -sensing receptors in intestinal epithelium"; <i>American Journal of Physiology</i> Vol. 273, No. 4, C1168-C1175 (Oct. 1997)		
al. "Effect of Several Hydrophilic Polymers on the Permeation of Morphine and Salicylic Acid through irless Rat Skin"; <i>Chem. Pharm. Bull.</i> 46(5) 882-885 (1998)		
"Permeability of Human Isolated Airways Increases after Hydrogen Peroxide and Poly-L-arginine"; <i>Am.</i> <i>Crit. Care Med.</i> Vol 153 pp. 841-846 (1996)		
yashi, "Composition for Transmucosally Absorbable Preparation"; Patent Abstracts of Japan, Publication 738, Publication Date April 4, 1998		
"Protamine Selectively Inhibits Collagen Synthesis by Human Intestinal Smooth Muscle Cells and Other mal Cells"; <i>Journal of Cellular Physiology</i> 140:463-470 (1989)		
et al. "Polyamino Acid Enhancement of Bacterial Phagocytosis by Human Polymorphonuclear s and Peritoneal Macrophages"; <i>Infection and Immunity</i> Vol. 43, No. 2, pp. 561-566 (Feb. 1984)		
t al., "Inflammatory responses induced by poly-L-arginine in rat lungs <i>in vivo</i> "; <i>Agents Actions</i> Vol. 39, p. 104-110 (1993)		
. "Mammalian urinary bladder permeability is altered by cationic proteins modulation by divalent <i>American Journal of Physiology</i> Vol. 267, No. 4, Part 1, pp. C1013-C1026 (1994)		
l., "Modification of Epithelial Permeability by Cationic Polypeptides"; <i>American Journal of Physiology</i> No. 6, Part 1, pp. C1637-C1647 (1993)		
. al., "Cationic Proteins Increase the Permeability of Cultured Rabbit Tracheal Epithelial Cells: ion by Heparin and Extracellular Calcium: <i>Experimental Lung Research</i> Vol. 22, No. 1, pp. 85-99 (1996)		
. "synthesis of Oligoarginine-Oligonucleotide Conjugates and Oligoarginine-Bridge Oligonucleotide <i>conjugate Chem.</i> Vol. 5, pp. 468-474 (Sept./Oct. 1994)		
DATE CONSIDERED		

RECEIVED
OCT 08 2002
TECH CENTER 1600/2900